AMENDMENTS TO THE CLAIMS

Please amend the claims as noted below, without prejudice to subsequent renewal. The listing of claims below replaces all prior versions, and listings, of claims in the application.

These amendments introduce no new matter and support for the amendment is replete throughout the specification and claims as originally filed. These amendments are made without prejudice and are not to be construed as abandonment or dedication of the previously claimed subject matter, or agreement with any objection or rejection of record.

Listing of Claims:

1. (Currently amended) A method of identifying a compound that reduces whole body insulin sensitivity of an animal, said method comprising: (a) administering a compound to a non-human animal, isolated tissue or isolated cell having reduced expression of functional Cbl compared to an otherwise isogenic wild-type animal, tissue or cell; and (b) determining a Cbl-associated phenotype selected from the group consisting of: (i) the activity of acetyl CoA carboxylase (ACC) and/or amount of phosphorylated ACC enzyme; (ii) the activity of AMP-dependent protein kinase (AMPK) and/or amount of phosphorylated AMPK enzyme; (iii) expression of mitochondrial uncoupling protein 3 (UCP3); (iv) free fatty acid level and/or fatty acid oxidation; (v) fat content; (vi) lean muscle mass; (vii) muscle thermogenesis; (viii) feeding behavior; (ix) the level of an insulin receptor (IR); (x) whole body energy expenditure; (xi) metabolic rate; and (xii) glucose tolerance in the animal, tissue or cell wherein a reduced amount of phosphorylated ACC enzyme, AMPK enzyme, amount of phosphorylated AMPK enzyme, expression of UCP3, fatty acid oxidation, lean muscle mass, muscle thermogenesis, feeding behaviour, IR level, whole body energy expenditure, metabolic rate or glucose tolerance, and/or enhanced activity of an ACC enzyme, free fatty acid level or fat content compared to the amount of phosphorylated ACC enzyme or activity of an ACC enzyme of a Cbl-deficient animal, tissue or cell to which the compound has not been administered indicates that the compound reduces whole body insulin sensitivity in an animal.

2-23. (Cancelled)

24. (Currently amended) A method of identifying a compound that enhances whole body insulin sensitivity of an animal comprising: (a) administering a compound to a non-human animal, isolated tissue or isolated cell expressing a functional Cbl protein and determining a Cbl-associated phenotype selected from the group consisting of: (i) the activity of acetyl CoA carboxylase (ACC) and/or amount of phosphorylated ACC enzyme; (ii) the activity of AMP-dependent protein kinase (AMPK) and/or amount of phosphorylated AMPK enzyme; (iii) expression of mitochondrial uncoupling protein 3 (UCP3); (iv) free fatty acid level and/or fatty acid oxidation; (v) fat content; (vi) lean muscle mass; (vii) muscle thermogenesis; (viii) feeding behavior; (ix) the level of an insulin receptor (IR); (x) whole body energy expenditure; (xi) metabolic rate; and (xii) glucose tolerance (b) determining the said Cbl-associated phenotype ~~the activity of ACC and/or amount of phosphorylated ACC enzyme~~ in a non-human animal, isolated tissue or isolated cell having reduced expression of functional Cbl compared to an otherwise isogenic wild-type animal, tissue or cell; and (c) comparing the said Cbl-associated phenotype ~~the activity of ACC and/or amount of phosphorylated ACC enzyme~~ at (a) and (b) wherein a phenotype associated with Cbl-deficiency at (a) selected from the group consisting of (i) increased activity of acetyl CoA carboxylase (ACC) and/or amount of phosphorylated ACC enzyme; (ii) increased activity of AMP-dependent protein kinase (AMPK) and/or amount of phosphorylated AMPK enzyme; (iii) increased expression of UCP3; (iv) reduced free fatty acid level and/or increased fatty acid oxidation; (v) reduced fat content; (vi) increased lean muscle mass; (vii) increased muscle thermogenesis; (viii) increased feeding behavior; (ix) increased level of an insulin receptor (IR); (x) increased whole body energy expenditure; (xi) increased metabolic rate; and (xii) increased glucose tolerance ~~comparable activity and/or amount of phosphorylated ACC enzyme between (a) and (b)~~ indicates that the compound enhances whole body insulin sensitivity of an animal.

25. (Original) The method of claim 24 wherein ACC activity is determined by a process comprising by measuring the incorporation of labeled carbon into malonyl CoA in the presence and absence of the compound.

26. (Currently amended) The method of claim 24 ~~claim 23~~ wherein phosphorylated ACC is determined by contacting cells or a cell extract with an antibody that binds to the phosphorylated form of the enzyme under conditions sufficient for an antigen-antibody complex to form and detecting the antibody bound.

27. (Original) The method of claim 26 further comprising separately contacting cells or cell extract with an antibody that binds to non-phosphorylated ACC under conditions sufficient for an antigen-antibody complex to form and detecting the antibody bound.

28. (Currently amended) The method of claim 26 ~~or 27~~ wherein detecting the antibody bound comprises contacting the antibody with a secondary antibody that is capable of producing a detectable signal.

29. (Currently amended) The method of claim 24 ~~claim 23~~ further comprising determining the percentage of phosphorylated ACC relative to total ACC in the sample in the presence and absence of the compound being tested.

30. (Currently amended) The method according to claim 24 ~~claim 23~~ wherein the non-human animal is a mammal.

31. (Original) The method according to claim 30 wherein the mammal is selected from the group consisting of rodent, dog, pig, bovine, sheep, horse and goat.

32. (Original) The method according to claim 31 wherein the rodent is selected from the group consisting of rabbit, rat, guinea pig and mouse.

33. (Original) The method according to claim 32 wherein the rodent is a mouse.

34. (Currently amended) The method of claim 24 ~~claim 23~~ wherein the cells are skeletal muscle cells, cardiac myoblasts or adipocytes.

35. (Currently amended) The method according to claim 24 ~~claim 23~~ wherein the animal, tissue or cell expresses an endogenous functional Cbl.

36. (Currently amended) The method of claim 24 ~~claim 23~~ wherein the animal, tissue or cell expresses and introduced Cbl gene.

37. (Original) The method of claim 36 wherein the animal, tissue or cell is non-human and expresses an introduced human Cbl gene.

38. (Currently amended) The method according to claim 24 ~~claim 23~~ wherein the compound being tested is a peptidyl inhibitor of Cbl.

39. (Original) The method of claim 38 wherein the inhibitor is a dominant negative mutant of Cbl.

40. (Cancelled)

41. (Currently amended) The method according to claim 24 ~~claim 23~~ wherein the compound being tested comprises nucleic acid.

42-43. (Cancelled)

44. (Currently amended) The method according to claim 24 ~~claim 23~~ wherein the compound is administered to muscle tissue of an animal subject.

45. (Currently amended) The method of claim 24 ~~claim 23~~ further comprising:
(i) optionally, determining the structure of the compound; and
(ii) providing the compound or the name or structure of the compound.

46. (Original) The method of claim 45 comprising providing the compound or the name or structure of the compound with an indication as to its use.

47. (Original) The method of claim 45 further comprising producing or synthesizing the compound.

48-71. (Cancelled)

72. (Currently amended) The method of claim 24 ~~claim 71~~ wherein AMPK activity is determined by a process comprising following the incorporation of labelled phosphate into a synthetic peptide SAMS in the presence and absence of the compound.

73. (Currently amended) The method of claim 24 ~~claim 71~~ wherein phosphorylated AMPK is determined by contacting cells or a cell extract with an antibody that binds to the phosphorylated form of the enzyme under conditions sufficient for an antigen-antibody complex to form and detecting the antibody bound.

74. (Original) The method of claim 73 further comprising separately contacting cells or cell extract with an antibody that binds to non-phosphorylated AMPK under conditions sufficient for an antigen-antibody complex to form and detecting the antibody bound.

75. (Currently amended) The method of claim 73 ~~or 74~~ wherein detecting the antibody bound comprises contacting the antibody with a secondary antibody that is capable of producing a detectable signal.

76. (Currently amended) The method of claim 24 ~~claim 71~~ further comprising determining the percentage of phosphorylated AMPK relative to total AMPK in the sample in the presence and absence of the compound being tested.

77-96. (Cancelled)

97. (Original) A method of identifying a therapeutic target for the treatment of aberrant insulin action or a condition associated therewith, said method comprising administering to an animal, tissue or cell a compound capable of reducing the expression and/or activity of a Cbl protein and determining the activity and/or expression of one or more genes and/or proteins in the animal, tissue or cell wherein modified expression and/or activity of a gene or protein indicates that the gene or protein is a therapeutic target for the treatment of aberrant insulin action or a condition associated therewith.

98-112. (Cancelled)

113. (Original) The method of claim 97 further comprising identifying a compound that modulates the expression or activity of the therapeutic target.

114. (Currently amended) A method of identifying a compound that enhances free fatty acid synthesis or reduces a member selected from the group consisting of: (i) mitochondrial acetyl CoA carboxylase (ACC) enzyme activity; (ii) mitochondrial AMP kinase (AMPK) enzyme activity; (iii) expression of mitochondrial uncoupling protein 3 (UCP3); (iv) fatty acid oxidation; and (v) expression of an insulin receptor (IR), said method comprising determining the level of Cbl expression and/or activity in the presence and absence of the compound wherein enhanced expression and/or activity of Cbl in the presence of the

compound indicates that the compound enhances free fatty acid synthesis or reduces a said member ~~mitochondrial ACC enzyme activity~~.

115. (Currently amended) A method of identifying a compound that reduces free fatty acid synthesis or enhances a member selected from the group consisting of: (i) mitochondrial acetyl CoA carboxylase (ACC) enzyme activity; (ii) mitochondrial AMP kinase (AMPK) enzyme activity; (iii) expression of mitochondrial uncoupling protein 3 (UCP3); (iv) fatty acid oxidation; and (v) expression of an insulin receptor (IR), said method comprising determining the level of Cbl expression and/or activity in the presence and absence of the compound wherein reduced expression and/or activity of Cbl in the presence of the compound indicates that the compound reduces free fatty acid synthesis or enhances a said member ~~mitochondrial ACC enzyme activity~~.

116-125. (Cancelled)

126. (Currently amended) The method according claim 114 ~~to any one of claims 114 to 125~~ wherein Cbl expression or activity is determined by a process comprising performing an immunoassay.

127. (Currently amended) The method according to claim 114 ~~claim 126~~ comprising determining the amount of Cbl protein in the cell in the presence and absence of the compound.

128. (Original) The method of claim 114 comprising determining the level of c-Cbl-mediated ubiquitination of the insulin receptor in the presence and absence of the compound.

129. (Currently amended) The method according to claim 114 ~~any one of claims 114 to 125~~ wherein Cbl expression or activity is determined by a process comprising determining phosphorylation of a tyrosine residue on Cbl protein in the presence and absence of the compound.

130. (New) The method according claim 115 wherein Cbl expression or activity is determined by a process comprising performing an immunoassay.

131. (New) The method according to claim 115 comprising determining the amount of Cbl protein in the cell in the presence and absence of the compound.

132. (New) The method of claim 115 comprising determining the level of c-Cbl-mediated ubiquitination of the insulin receptor in the presence and absence of the compound.

133. (New) The method according to claim 115 wherein Cbl expression or activity is determined by a process comprising determining phosphorylation of a tyrosine residue on Cbl protein in the presence and absence of the compound.

134. (New) A method for identifying a compound that enhances insulin sensitivity and/or energy expenditure of an animal comprising determining the level of Cbl expression and/or activity in the presence and absence of the compound wherein reduced expression and/or activity of Cbl in the presence of the compound indicates that the compound enhances insulin sensitivity and/or energy expenditure.

135. (New) The method according claim 134 wherein Cbl expression or activity is determined by a process comprising performing an immunoassay.

136. (New) The method according to claim 134 comprising determining the amount of Cbl protein in the cell in the presence and absence of the compound.

137. (New) The method of claim 134 comprising determining the level of c-Cbl-mediated ubiquitination of the insulin receptor in the presence and absence of the compound.

138. (New) The method according to claim 134 wherein Cbl expression or activity is determined by a process comprising determining phosphorylation of a tyrosine residue on Cbl protein in the presence and absence of the compound.

139.. (New) A method for identifying a compound that reduces insulin sensitivity and/or energy expenditure of an animal comprising determining the level of Cbl expression and/or activity in the presence and absence of the compound wherein reduced expression and/or activity of Cbl in the presence of the compound indicates that the compound reduces insulin sensitivity and/or energy expenditure.

140. (New) The method according claim 139 wherein Cbl expression or activity is determined by a process comprising performing an immunoassay.

141. (New) The method according to claim 139 comprising determining the amount of Cbl protein in the cell in the presence and absence of the compound.

142. (New) The method of claim 139 comprising determining the level of c-Cbl-mediated ubiquitination of the insulin receptor in the presence and absence of the compound.

143. (New) The method according to claim 139 wherein Cbl expression or activity is determined by a process comprising determining phosphorylation of a tyrosine residue on Cbl protein in the presence and absence of the compound.

144. (New) A method of treatment of an animal or human subject for a condition associated with aberrant insulin action said method comprising administering to the subject an effective amount of a compound that modulates ACC activity and/or AMPK activity and/or FFA level and/or fatty acid oxidation and/or Cbl expression or activity thereby treating a condition associated with aberrant insulin action.

145. (New) The method of claim 144 wherein the condition is selected form the group consisting of hyperglycemia, hyperinsulinemia, obesity, adult-onset obesity, non-insulin-dependent diabetes mellitus, type II diabetes, glucose intolerance, hypertrophy or hyperplasia of the islets of Langerhans, atherosclerosis and heart disease.